REMARKS

The Amendments

The claims are amended to address the objections and 35 U.S.C. §112 rejections.

It is submitted that the above amendments would put the application in condition for allowance or materially reduce or simplify the issues for appeal. The amendments do not raise new issues or present new matter and do not present additional claims. The amendments have been made to address the objections and 35 U.S.C. §112 rejections, including rejections made for the first time in the Final action. Thus, they were not earlier presented. Accordingly, it is submitted that the requested amendments should be entered. At the least, the amendments render moot many of the objections/rejections and, thus, should be entered at least for purposes of appeal.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Objection to the Specification

The specification has been corrected as noted in the Office Action.

The Claim Objection

The amendment to claim 22 renders the objection moot.

The Rejections under 35 U.S.C. §112

The rejection of claim 30 under 35 U.S.C. §112, second paragraph, is rendered moot by the above amendment. The specification at page 51 and page 36-37 and the knowledge of one of ordinary skill in the art makes it clear that the β term is correct.

The rejection of claims 9, 13, 14 and 22-33 under 35 U.S.C. §112, first paragraph, is rendered moot by cancellation of the "solvate" term.

The rejection of claim 31 under 35 U.S.C. §112, second paragraph, is believed to be rendered moot by the amendment thereto. The claim is amended to incorporate the language from claim 14 (which was not subject to such rejection). The claim thus now clarifies the specific activity of the

PDE VII isozyme that is connected with the disease or disorder, i.e., the PDE VII isozyme role in regulating the activation and degranulation of human eosinophils. This specific role of the PDE VII isozyme is more fully discussed at pages 5-6 of the instant specification. Based on this discussion and the knowledge of one of ordinary skill in the art, the reader of ordinary skill in the art can reasonably ascertain the scope and meaning of the claim.

The rejection of claim 33 under 35 U.S.C. §112, second paragraph, is believed to be rendered moot by the amendment thereto removing the extraneous "coronary" term.

The rejections of claims 32 and 33 under 35 U.S.C. §112, first paragraph, for lack of enablement, are respectfully traversed. These rejections will be discussed together since many of the issues are common but any distinctions relating to claim 32 or 33 will be pointed out.

It is believed that these rejections may be rendered moot by the amendments thereto whereby they are made dependent on amended claim 31. Thus, the claims are not directed to treating any manner of the diseases recited therein but only the diseases or disorders in these categories which are "caused by the PDE VII isozyme in its role in regulating the activation and degranulation of human eosinophils." As discussed above for claim 31, this specific role of the PDE VII isozyme is more fully discussed at pages 5-6 of the instant specification and gives one of ordinary skill in the art excellent guidance in the nature of the activity provided by the compounds to treat diseases or disorders connected to such activity.

Applicants note application of the "Wands" factors and discuss these below, however, applicants urge that the "Wands" factors are not the only consideration. It must also be considered that, to support a lack of enablement rejection, the burden lies first with the PTO to provide evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. See, e.g., In re Marzocchi et al., 169 USPQ 367 (CCPA 1971), stating:

> ".. a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein..",
> and further,

> "..it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." (emphasis original).

Applicants submit that no clear case with supporting evidence has been set forth for why the PTO doubts the statements of the inventors as to how the claimed invention can be used. Further, applicants urge that the standard for enablement is not absolute predictability but only reasonable expectation of success; see In re Wright, 999 F.2d 1557, 27 USPQ2d 1510,1512 (Fed.Cir. 1993).

As for the "Wands" factors, applicants have the following comments and submit that, considered as a whole, they do not weigh in favor of non-enablement.

A) Breadth of Claims - The breadth of claims regarding the compounds used is very narrow which strongly weighs in favor of enablement. The breadth of the claims as to the diseases or disorders being treated is fairly broad in claim 32 but quite specific in claim 33. Further, as to both claims, the scope is clarified by the recitation that the disease or disorder is connected with activity of the PDE VII isozyme in its role in regulating the activation and degranulation of human eosinophils. This activity is quite specific. (The Office Action discusses the scope of "enzymes" but it appears that this was intended to relate to "diseases.") The Office Action discusses that the potential diseases encompassed could be high but never provides any objective evidence or reasoning why one of ordinary skill in the art would not be able to practice the invention on such diseases, particularly in view of the clarification of the claims specifying the activity upon which the treatment is based.

B) The nature of the invention and predictability in the art - Applicants respectfully disagree with the conclusion in the Office Action that all inventions related to medicine or physiological activity are unpredictable. No objective reasoning or evidence has been provided to support that the physiological activity connected with the claimed invention was unpredictable. Further, absolute predictability is not required.

C) Direction or Guidance - The Office Action indicates that the failure to specify particular dosage ranges as to each specific sub-method shows non-enablement. Applicants respectfully submit

that, given the general guideline of the disclosure, one of ordinary skill in the art would need only routine experimentation to determine a dosage and administration regimen suited to the particular disease being treated. It is common and routine in the pharmaceutical arts to formulate a dosage given guidelines on the general dose range and the nature of the activity provided by the active ingredient. Further, the specification provides significant guidance, e.g., on the compounds' activity (pages 3-6), the compounds' preparation (pages 7-9 and 13-19), formulation and modes of administration for the compounds (pages 20-21 and 53-76), and particular applications (pages 26-37).

D) State of the Prior Art - The fact that the art fails to teach or suggest applicants' compounds as having such activity or for use in such treatment methods is part and parcel for why it is a patentable invention. The articles referred to, which teach potential uses for PDE VII inhibitors, do not provide any basis to doubt the inventors' teachings that their compounds have the stated uses. Again, the burden of proof is not being properly applied. The burden is on the PTO to provide evidence that raises a doubt that the compounds could reasonably be used as disclosed and claimed. The references speculate that the compounds would have certain uses but they give no indication that the compound would not be useful. As for the articles about unpredictability in being able to generally treat all cancers or other diseases, applicants respectfully submit that the claims are not as broad as alleged. The method claims are all directed to treating only those diseases or disorders caused by the PDE VII isozyme in its role in regulating the activation and degranulation of human eosinophils. One of ordinary skill in the art would be able to reasonably determine what diseases or disorders would fall within this recitation.

E) Working Examples - Although the specification does not contain working examples of actual methods of treatment, the law is clear that it is not necessary to provide working examples in order to enable the invention. See, e.g., In re Borkowski, 422 F.2d 904, 164 USPQ 642 (CCPA 1970); and, In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). Since the other factors are believed to, as a whole, weigh in favor of enablement, this one negative factor does not alone support lack of enablement.

F) Level of Skill of those in the Art - This factor relates the level of skill of those in the art, not what the prior art teaches (this was factor D) above). The level of skill of one of ordinary skill in

this art would be quite high. Researchers for new pharmaceuticals for these uses are at Ph.D. level and have a high level of skill. Thus, they would be well versed in, for example, the role of the PDE VII isozyme in regulating the activation and degranulation of human eosinophils and what diseases or disorders would be associated therewith.

G) Quantity of Experimentation - The quantity of experimentation needed is not decisive. A great deal of experimentation is acceptable as long as it is not undue. Enablement is found even where there is a large amount of routine experimentation. Applicants respectfully submit that given the guidance of their disclosure, the clarified claims, the knowledge in the art and the high level of skill of those in this art, that only routine experimentation would be needed to carry out the claimed methods.

For all of the above reasons, it is urged that one skilled in the art is reasonably taught how to make and use the claimed invention. Thus, the rejections for lack of enablement under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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